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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,663	01/18/2002	Vernon M. Ingram	M00656/70071 (JRV)	3098

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EXAMINER
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CELSA, BENNETT M

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary****Application No.**

10/051,663

**Applicant(s)**

INGRAM ET AL.

**Examiner**

Bennett Celsa

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 June 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 29, 34 and 49 is/are pending in the application.
- 4a) Of the above claim(s) 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29 and 49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

**Response to Amendment**

Applicant's amendment dated 6/24/04 is herein acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Status of the Claims**

Claims 29, 34 and 49 are currently pending.

Claims 29 and 49 are under consideration..

Claim 34 is withdrawn from consideration as being directed to a nonelected invention.

**Election/Restriction**

2. Applicant's election with traverse of Group V (claim 29: composition comprising an inhibitor of neural membrane depolarization and a compound that decrease neuronal calcium influx) and i. DAPH1 (4,5-dianilinophthalimide) as a compound species that decreases neuronal membrane depolarization of neuronal cells caused by aggregated beta-amyloid protein degradation products and ii. 2,3-dihydroxy-nitro-7-sulfamoyl-benzo[f]quinoxaline (NBQX) as the compound that decreases neuronal calcium influx in the correspondences dated 10/31/03 and 1/15/04, respectively, is acknowledged.

3. Claim 34 is withdrawn from consideration as being directed to a nonelected invention. It is noted that, in accordance with U.S. practice, the Examiner will *consider rejoinder* of a method of use (e.g. claim 34) which is commensurate in scope to allowed subject matter pursuant to MPEP 821.04 Rejoinder. However, a complete reply to the final rejection

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must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Withdrawn Objection (s) and/or Rejection (s)***

Applicant's amendment has overcome the rejection of Claim 29 under 35 U.S.C. 103(a) as being unpatentable over Buxbaum Pat No. 5,385,915 (1/95) alone or further in view of Ingram et al. PG PUB US 2003/0114510A1 (6/03) as evidence of inherency (item 8 in the prior office action) and further in view of WO 98/30229 (7/98) (item 10 in the prior office action).

***Outstanding Objection(s) and/or Rejection (s)***

4. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of written description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an

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invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

The *Lilly* court sets forth a two part test for written description: A description of a genus of cDNA's may be achieved by means of a recitation of:

1. a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or
2. of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

The present claim is directed to: A composition comprising:

- a. DAPH1 (4,5-dianilinophthalimide) AND
- b. one or more compounds that "*decrease neuronal calcium influx by beta amyloid protein degradation products*".

In support thereof of item b. above, the specification merely provides a handful of compounds corresponding to item b. (e.g. Non-NMDA channel antagonist compounds, decoy peptides) in which functional/mechanistic properties are not correlative to a single

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compound core structure. See e.g. Ingram et al. PG PUB US 2003/0114510A1 (6/03) (of present application) at pages 1-7.

In the present instance, neither the specification nor the claims provide:

1. A recitation of structural features common to the members of the "genera" corresponding to *"compounds that decrease neuronal calcium influx by beta amyloid protein degradation products"* OR
2. a representative number of compounds that decrease neuronal calcium influx caused by aggregated beta-amyloid protein degradation products..

Accordingly, neither the specification nor claims demonstrate possession of the presently claimed function/mechanistic claimed generics.

### ***Discussion***

Applicant's arguments directed to the above written description rejection (as modified in response to applicant's amendment) were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the specification provides an adequate written description of compounds that decrease calcium influx of neuronal cells caused by aggregated  $\beta$ -amyloid

(A $\beta$ ) protein degradation products since the specification describes:

- a. Decoy peptides (e.g. pp. 9,16);
- b. A number of non-NMDA antagonists (see pp 16-17); and

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c. Other antagonists of calcium channels (see page 16) including NMDA antagonists such as DL-AP5 (see Example 1, p. 30);

which, although structurally different, would nevertheless, given the knowledge in the art of these compounds, be viewed as representative of compounds that decrease calcium influx of neuronal cells caused by aggregated  $\beta$ -amyloid ( $A\beta$ ) protein degradation products.

This argument was considered but deemed nonpersuasive for the following reasons.

As recognized by the courts, "[T]he written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant, identifying characteristics ... i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics.'" *Enzo Biochem. Inc. V. Gen-Probe Inc.* 296 F.3d 1316,1324, 63 USPQ2d 1609,1613 (Fed. Cir. 2002).

In the present instance, Applicant's claimed composition comprising **compounds that decrease calcium influx of neuronal cells caused by aggregated  $\beta$ -amyloid**

**(A $\beta$ ) protein degradation products** which represents a “vague functional description”<sup>1</sup> which lacks any structural feature (e.g. core structure) common to compounds that decrease calcium influx; nor is there sufficiently detailed, relevant, identifying characteristics ... i.e. complete or partial structure, other physical and/or chemical properties to provide an adequate written description. Even though the specification provides specific examples of “decoy peptides” and an NMDA antagonist (e.g. DL-AP5) these compounds are structurally distinct and do not establish a known or disclosed correlation between function and structure sufficient to provide adequate written description; nor do these disclosed compound provide functional/mechanistic properties which are correlative to a single compound core structure(s).

Accordingly, as pointed out in the rejection above, applicant’s claim to a “vague functional description” and the limited numbers of specification examples fail to provide:

1. A recitation of structural features common to the members of the “genera” corresponding to *“compounds that decrease neuronal calcium influx by beta amyloid protein degradation products”* OR

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<sup>1</sup> The claimed phrase “a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product” was labeled by the CAFC as a “vague functional description”. See *University of Rochester v. G.D. Searle & Co.*, 69 USPQ 2d 1886,1895 (CAFC 2004).



2. a representative number of compounds that decrease neuronal calcium influx caused by aggregated beta-amyloid protein degradation products..

Thus, neither the specification nor claims provides an adequate written description of compounds that decrease calcium influx of neuronal cells caused by aggregated  $\beta$ -amyloid (A $\beta$ ) protein degradation products as presently claimed.

5. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buxbaum Pat No. 5,385,915 (1/95), Ingram et al. PG PUB US 2003/0114510A1 (6/03) {as evidence of inherency} and Sharpe et al., US Pat. No. 6,552,066 (4/03: filed 9/96 or earlier).

Claim 29 (as amended) is directed to: A composition comprising:

- a. DAPH1 (4,5-dianilinophthalimide) AND
- b. one or more compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*.

Buxbaum teaches the making of compositions comprising:

- a. one or more kinase inhibitors (e.g. tyrphostin) (e.g. see abstract; see col. 11, line 50; patent claims, especially claims 1, 2, 7, 17, 27 etc.) And
- b. one or more calcium modulators (e.g. glutamate) (e.g. see abstract; col. 11, lines 50-61, patent claims, especially claims 1, 8, 10, 20, 30 etc.)

for treating diseases associated with amyloid plaque deposition, especially Alzheimer's disease.

Additionally, Ingram et al. PG PUB discloses that non-NMDA channel antagonists, such as "glutamate" inherently *"decrease neuronal calcium influx by beta amyloid protein degradation products"*.

Accordingly, the Buxbaum reference provides explicit motivation for one of ordinary skill in the art to make (e.g. in its disclosure and patent claims) compositions comprising :

- a.. one or more kinase inhibitors (e.g. tyrphostin) and
- b. compound(s) that *"decrease neuronal calcium influx by beta amyloid protein degradation products" (including glutamate)*

in order to produce compositions for treating diseases associated with amyloid plaque formation (e.g. Alzheimer's disease).

To the extent that the Buxbaum reference fails to explicitly disclose the selection of DAPH1 (4,5-dinitrophthalimide) as a Tyrosine kinase inhibiting compound species, the Sharpe et al. reference is cited.

The Sharpe reference teaches that DAPH1 is a member of the Tyrosine kinase family of inhibitors, as disclosed in the Buxbaum reference, including tyrphostin and thus are expected to be functionally equivalent. E.g. See Sharpe at col. 2, lines 15-32; col. 4).

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to utilize DAPH1 as a kinase inhibiting compound in the Buxbaum reference composition since the Buxbaum reference discloses the use of various kinase inhibiting compounds in its compositions which would include DAPH1

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which is taught by the Sharpe reference to be a functionally equivalent member of the tyrosine kinase family of inhibitors which include similar functionally equivalent members (e.g. tyrphostin) as those disclosed in Buxbaum.

6. Claims 29 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buxbaum Pat No. 5,385,915 (1/95), Ingram et al. PG PUB US 2003/0114510A1 (6/03) {as evidence of inherency} and Sharpe et al., US Pat. No. 6,552,066 as applied to claim 29 above, and further in view of Ingram WO 98/30229 (7/98).

The combined teaching of the Buxbaum, Ingram(inherency) and Sharpe references as discussed in the rejection of claim 29 above is hereby incorporated by reference in its entirety.

To the extent that the Buxbaum reference fails to **explicitly** disclose the incorporation in its compositions of compounds that "*decrease neuronal calcium influx by beta amyloid protein degradation products*", which include "decoy peptides" or "non-NMDA channel antagonists" (e.g. claim 49: NBQX), the Ingram WO 98/30229 document is cited.

Ingram WO 98/30229 teaches compositions comprising compounds that "*decrease neuronal calcium influx by beta amyloid protein degradation products*" (e.g. "decoy peptides" : i.e.. see pages 4, 10-11, 14-15; and "Non-NMDA channel antagonists: see pages 17-18, especially page 17, lines 11-28 which include **NBQX**: see also examples and claims e.g. claims 22 and 27 ) for treating conditions

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characterized by unwanted beta-amyloid peptide aggregate formation including Alzheimer's disease.

Accordingly, one of ordinary skill in the art would have been motivated to incorporate in the Buxbaum reference compositions the Ingram WO 98 "decoy peptide" or Non-NMDA antagonist compounds (e.g. NBQX) that *"decrease neuronal calcium influx by beta amyloid protein degradation products"* since:

- a. Buxbaum teaches the incorporation of calcium channel modulating compounds (e.g. see patent claims, especially claim 10, 26, 30 etc. and "glutamate" ; and
- b. The Buxbaum and Ingram WO 98 reference compositions are made for the same purpose e.g. the treatment of diseases (e.g. Alzheimer's disease) associated with amyloid plaque aggregation.

See also *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate into the Buxbaum reference composition compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*, which include "decoy peptides" or Non-NMDA calcium channel antagonists (e.g. NBQX) as taught by Ingram WO 98 with a reasonable expectation of achieving compositions within the scope of the presently claimed invention.

### ***Discussion***

Applicant's arguments directed to the above obviousness rejections (which were modified in response to applicant's amendment) were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the Buxbaum reference fails to teach DAPH1.

In response to applicant's arguments against the Buxbaum reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the Ingram application is not prior art to the instant application, and should not serve as evidence of inherency of these compounds, since the effect of tyrphostin (the compound cited by the Examiner) on membrane depolarization, is Applicant's discovery. Applicant further argues that "[C]iting Applicant's own later-filed application as evidence of inherency of Applicant's own invention should not be a sufficient basis for an obviousness rejection as made here.

Applicant's arguments were considered but deemed nonpersuasive for the following reasons.

The citation of a reference, or any means of extrinsic evidence to demonstrate inherency, is permitted (e.g. see MPEP 2131.01), in which the date of the extrinsic evidence need not antedate the filing date (e.g. see MPEP 2124). In fact, use of applicant's own specification, as the source of extrinsic evidence is permitted. E.g. see

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*Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993) (use of application example to demonstrate inherency).

Even assuming *arguendo* that the prior art failed to disclose or suggest a "latent" or "inherent" property, the case law recognizes time and again that "mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention". See *In re Wiseman*, 596 F.2d. 1019, 201 USPQ 658 (CCPA 1979). For granting a patent on the discovery of an unknown but inherent function "would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. See 201 USPQ at 661; *In re Baxter*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only that the subject matter is in fact inherent in the prior art reference. See *Schering Corp. V. Geneva Pharm. Inc.* 339 F.3d 1373,1377, 67 USPQ2d 1664,1668 (Fed. Cir. 2003); see also MPEP 2112-2112.02.

In response to the Ingram (US 2003/01145110A1) reference, Applicant further argues that "[C]iting Applicant's own continuation-in-part application as providing the connection to two compounds, in Buxbaum alone ... or in Buxbaum and Sharpe ... is improper. Thus there is no legally sufficient motivation to select the specific claimed compounds as claimed by Applicant, or to combine the cited references."

These arguments were considered but deemed nonpersuasive for the following reasons.

Applicant's argument is misguided since it is clear from the above rejections that the Ingram (US 2003/01145110A1) document is being properly used solely as evidence of inherency and NOT as motivation to select claimed compounds or for motivation to combine references. Motivation to select the presently claimed compounds (with their inherent properties) and combine references is provided for in the prior art references (e.g. Buxbaum and Sharpe) as clearly pointed out in the above obviousness rejections.

Regarding the Sharpe et al. reference teaching of DAPH1, applicant argues that "the Examiner's assertion regarding the functional equivalency of DAPH1 and other tyrosine kinase inhibitors is too broad. While DAPH1 and tyrphostin both are tyrosine kinase inhibitors, Sharpe only teaches or suggests to one of ordinary skill in the art that these compounds are functionally equivalent for inhibiting tyrosine kinase activity, not anything else."

This argument was considered, but deemed nonpersuasive, for the following reasons.

In response to applicant's arguments against the Sharpe and Buxbaum reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the present instance, the above obviousness rejections are directed to the combined Buxbaum and Sharpe teaching. As pointed out in the above obviousness rejections:

1. the Buxbaum reference provides explicit motivation for one of ordinary skill in the art to make (e.g. in its disclosure and patent claims) compositions comprising *one or more kinase inhibitors (e.g. tyrphostin)* for treating diseases associated with amyloid plaque formation (e.g. Alzheimer's disease); and

2. The Sharpe reference teaches that DAPH1 is a member of the Tyrosine kinase family of inhibitors, as disclosed in the Buxbaum reference, including tyrphostin and thus are expected to be functionally equivalent. E.g. See Sharpe at col. 2, lines 15-32; col. 4).

Accordingly, obviousness results from the combination of the two reference teachings with the substitution in the Buxbaum reference therapeutic composition of one kinase inhibitor (e.g. tyrphostin) for another functionally equivalent one being obvious since, as admitted by applicant, one of ordinary skill in the art would deem that these compounds are functionally equivalent for inhibiting tyrosine kinase activity and thus substitutable for one another in the Buxbaum reference compositions. It is noted that an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist. See *In re Scott*, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963). Additionally, functional equivalency as presented in the obviousness rejection(s) above, is proper insofar that the equivalency is recognized in the prior art, and is NOT based on applicant's disclosure. See *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958). Further, obviousness based on functional equivalency does NOT require an express suggestion to substitute one equivalent component or process for another to render such substitution obvious. See *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).



In response to the citation of the Ingram PCT application as teaching decoy peptides and non-NMDA channel antagonists as compounds that decrease neuronal calcium influx by beta-amyloid degradation products applicant argues that "there is no motivation for one of ordinary skill in the art to select and combine the claimed compounds without the benefit of Applicant's disclosure, i.e., this rejection is based on hindsight. Without more, one of ordinary skill in the art in reading the Buxbaum patent would not be motivated to combine a compound as taught by Buxbaum (which is not DAPH1) with another compound as taught by the Ingram PCT application."

This argument was considered but deemed nonpersuasive for the following reasons.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The above obviousness rejections do not constitute improper hindsight reconstruction since the above rejections take into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, as disclosed in the references, and does not include knowledge gleaned only from the

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applicant's disclosure. More particularly, regarding the Buxbaum and WO 98 references, the above obviousness rejection clearly points out that one of ordinary skill in the art would have been motivated to incorporate in the Buxbaum reference compositions the Ingram WO 98 "decoy peptide" or Non-NMDA antagonist compounds (e.g. NBQX) that *"decrease neuronal calcium influx by beta amyloid protein degradation products"* since:

- a. Buxbaum teaches the incorporation of calcium channel modulating compounds (e.g. see patent claims, especially claim 10, 26, 30 etc. and "glutamate" ; and
- b. The Buxbaum and Ingram WO 98 reference compositions are made for the same purpose e.g. the treatment of diseases (e.g. Alzheimer's disease) associated with amyloid plaque aggregation.

Additionally, as pointed out above, it is clear from the above rejections that the Ingram (US 2003/01145110A1) document is being properly used solely as evidence of inherency and NOT as motivation to select claimed compounds or for motivation to combine references and as such does not constitute improper hindsight reconstruction.

Accordingly, the above obviousness rejections, as modified, are hereby maintained.

***Cumulative Relevant Prior Art:***

The following two references teach the CNS (e.g. brain and spinal cord) neuroprotective effect of the non-NMDA antagonist NBQX:

A. Dalgaard, WO 94/22446 (10/94).

B. Olney, US Pat. No. 5,834,465 (11/98).

**Conclusion**

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

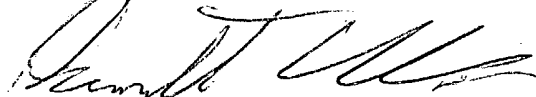
**Future Correspondences**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa  
Primary Examiner  
Art Unit 1639



BC  
September 9, 2004